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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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09/139,058 08/24/98 WOODLE

M 5335-0122-20
EXAMINER

022918 HM22/0621
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ART UNIT PAPER NUMBER
KISHORE, G

DATE MAILED:

06/21/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 4-10-00
- ☒ This action is **FINAL**.

- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 8-9 & 11-19 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 8-9 & 11-19 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s) _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

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DETAILED ACTION

The request for the extension of time, amendment and power of attorney filed on 4-10-00 are acknowledged.

Claims included in the prosecution are 8-9 and 11-19.

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 8-9 and 11-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff ((4,897,384) or Popescu (4,981,692) in view of Yoshioka (5,593,622).

Janoff teaches gentamycin containing liposomes (note the abstract, examples and claims). Janoff however, does not teach that the phospholipids used in the formation of liposomes be attached with the hydrophilic polymer such as polyethylene glycol (PEG).

As pointed out above, Popescu teaches liposome formulations containing gentamycin. Popescu although teaches that cholesterol-PEG could be used in the liposomes, does not teach that phospholipids used in the formation of liposomes be attached with the hydrophilic polymer, polyethylene glycol (PEG).

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Yoshioka teaches that when phospholipids which are attached to PEG are used in the formation of liposomes, the hydrophilic moiety of PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes (note the abstract). In essence Yoshioka indirectly teaches that the stability of the liposomes is increased.

The attachment of PEG to the surface of the liposomes (by coupling with the phospholipid) taught by Janoff or Popescu would have been obvious to one of ordinary skill in the art because PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes as taught by Yoshioka.

Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants once again argue that the important feature of the Janoff preparation appears to be the ability of the selected ligand to competitively bind with the toxicity receptor and that the modification of the phospholipid head group with a PEG chain will prevent such a binding. This argument is not found to be persuasive since Janoff on columns 15-17 teaches liposomes containing PEG-cholesterol in the preparation of liposomes and if applicant's reasoning that modification of the liposomal surface by attachment with PEG would prevent the binding of the drug and thus defeating the purpose for which it is used for in the prior art, then the examiner points out that Janoff would not have suggested the use of PEG at all. The examiner also points out that cholesterol being lipophilic, just like other amphiphilic lipids, it would be associated with

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the membrane of the liposomes and PEG in PEG-cholesterol taught by Janoff would naturally be exposed on the surface of the liposomes. Therefore, one skilled in the art would be motivated to attach PEG to an amphiphilic lipid since the secondary reference clearly teaches that PEG increases the stability of the liposomes. The examiner also points out the motivation for one to use PEG need not be the same as applicant's.

Applicants' arguments once again that Popescu is concerned with RES are not found to be persuasive. These have been addressed before. As pointed out before, on columns 4 and 5 Popescu only refers to the sites the bacteria is likely to infect. On column 5, line 42 et seq., Popescu clearly teaches that his invention is not limited to the treatment of intracellular infections, but can be "*directed to a variety of sited of infection whether intracellular or extracellular*". Furthermore, as pointed out before, Popescu also advocates on col. 4, lines 7-8 the use of PEG-cholesterol which substantiates that Popescu's compositions are meant to treat infections irrespective of the site of infection. Therefore, one skilled in the art would use PEG since according to the secondary reference, it increases the stability of the liposomes. As pointed out above, the motivation to use PEG need not be the same as applicants'.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is

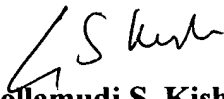
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more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.


Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

June 20, 2000